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EXAMINER	
WOOLWINE, SAMUEL C	
ART UNIT	PAPER NUMBER
1637	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,840	DRESSMAN ET AL.	
	Examiner	Art Unit	
	SAMUEL WOOLWINE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *1-34,55-58 and 80-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-54 and 59-79* is/are rejected.

7)☒ Claim(s) *64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :12/29/2005;02/09/2006;06/19/2007;07/05/2007.

DETAILED ACTION

Status

This application has been transferred to examiner Samuel Woolwine, whose contact information appears below.

Election/Restrictions

Applicant's election of Group III, claims 35-54 and 59-79, in the reply filed on 06/27/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-34, 55-58 and 80-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/27/2008.

The requirement for restriction is made FINAL.

Information Disclosure Statement

The information disclosure statement filed 06/19/2007 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because paper copies of the foreign patent documents were not provided. The letter accompanying the IDS states that these references were provided on an enclosed compact disk. MPEP 609.04(a)(II) states:

> Electronic means or medium for filing IDSs are not permitted except for: (A) citations to U.S. patents and U.S. patent application publications in an IDS filed via the Office 's Electronic Filing System (EFS) (see MPEP § 609.07); or (B) a compact disc (CD) that has tables, sequence listings, or program listings included in a paper IDS in compliance

> with 37 CFR 1.52(e). A CD cannot be used to submit an IDS listing or copies of the documents cited in the IDS.

The IDS has been placed in the application file, but the foreign patent documents referred to therein have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

The information disclosure statement filed 12/29/2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because paper copies of the foreign patent documents and non-patent literature were not provided. The letter accompanying the IDS states that these references were cited in the International Search Report. MPEP 609.04(a)(II) states (with emphasis provided):

> There are exceptions to this requirement that a copy of the information must be provided. First, 37 CFR 1.98(d) states that a copy of any patent, publication, pending U.S. application, or other information listed in an information disclosure statement is not required to be provided if: (A) the information was previously cited by or submitted to, the Office in a prior application, provided that the prior application is properly identified in the IDS and is relied on for an earlier filing date under 35 U.S.C. 120; and (B) the IDS submitted in the earlier application complies with 37 CFR 1.98(a)-(c). If both of these conditions are met, the examiner will consider the information previously cited or submitted to the Office and considered by the Office in a prior application relied on under 35 U.S.C. 120. <u>This exception to the requirement for copies of information does not apply to information which was cited in an international application under the Patent Cooperation Treaty</u>.

The IDS has been placed in the application file, but only the US patent documents have considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for

purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

Claim 64 is objected to because of the following informalities: the phrase "thereby amplifying of the nucleic acid molecule" appears to contain a typographical error; the word "of" should be removed. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 79 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 79 recites the limitation "on a plurality of the reaction chambers" in step (e). There is insufficient antecedent basis for this limitation in the claim; there is no previous recitation of any "reaction chambers".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 70-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghadessy et al (PNAS 98(8):4552-4557, April 2001, cited on the IDS of 02/09/2006).

With regard to claim 70, Ghadessy teaches:

(a) forming aqueous compartments in a water-in-oil emulsion, wherein a plurality of the compartments include a nucleic acid molecule, and an aqueous solution comprising components necessary for nucleic acid amplification;

(b) amplifying the nucleic acid molecule in the compartments to form amplified copies of the nucleic acid molecule.

See figure 1 and page 4553, column 2, "Results and Discussion", "Principles Underlying CSR". Ghadessy teaches a method wherein *E. coli* cells (harboring plasmids encoding various polymerase genes) were mixed with the reactants required for nucleic acid amplification. Then the mixture was emulsified to form a water in oil emulsion, where the individual droplets of the aqueous phase contained single cells (see page 4553, last full sentence) and the nucleic acids were amplified.

With regard to claim 71, although Ghadessy uses the term CSR, the amplification is clearly a PCR reaction (see page 4553, column 1, "Selection": 20 cycles of 94°C for 1 min, 55°C for 1 min, and 72°C for 5 min).

With regard to claim 72, Ghadessy states the emulsion was heat stable (column 2, "Results and Discussion", "Principles Underlying CSR").

Claims 35-38, 40-41, 44-52, 54, 59-61 and 63-79 are rejected under 35 U.S.C. 102(e) as being anticipated by Leamon et al (U.S. Patent 7,323,305). On 5/30/2006, the application which issued as the '305 patent (application serial no. 10/767,779) was granted a petition to receive a change in the filing date from 22 September 2004 to 28 January 2004. The '305 patent claims priority to, among other provisional applications, provisional application 60/476,504 (filed June 6, 2003) and 60/465,071 (filed April 23, 2003).

With regard to claim 35, Leamon teaches a method comprising:

forming microemulsions comprising one or more species of analyte DNA molecules;

See claim 1: "delivering the fragmented nucleic acids into aqueous microreactors in a water-in-oil emulsion such that a plurality of aqueous microreactors comprise a single copy of a fragmented nucleic acid".

amplifying analyte DNA molecules in the microemulsions in the presence of reagent beads, wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule;

See claim 1: "amplifying the fragmented nucleic acids in the microreactors to form amplified copies of said nucleic acids and binding the amplified copies to beads in the microreactors". See figure 6, and column 20, line 28 through column 21, line 20.

separating the product beads from analyte DNA molecules which are not bound to product beads;

See figure 1G, at "Sequencing" step, "Second Strand Removal".

determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads.

See claim 1: "performing a sequencing reaction simultaneously on a plurality of the reaction chambers".

With regard to claim 36, Leamon teaches delivering the product beads to an array of reaction chambers, such that each chamber receives a single product bead. Hence, a bead bound to copies of one nucleic acid species is separated from a bead bound to copies of a second nucleic acid species. See claim 1.

With regard to claim 37, Leamon teaches that empty beads can be separated from beads bound to copies of amplified product using a fluorescence cell sorter (column 27, lines 31-51) before delivering the beads to the array of chambers. Hence the step of isolating is performed "using" fluorescence activated cell sorting.

With regard to claims 38 and 40, see column 24, lines 46-54: "Alternatively, the beads may be isolated and the DNA may be removed from each bead and sequenced."

With regard to claim 41, see column 25, lines 57-60, where Leamon teaches that using a fragment to bead ratio of 0.1, 9% of the beads would end up having one amplicon, whereas 0.5% of the beads would end up having more than one amplicon. 9.5% is less than 10%.

With regard to claim 44, the method set forth in Leamon's claim 1 would inherently satisfy the limitations. Given the fact that the beads are distributed to an array of 10,000 or more reaction chambers and are simultaneously sequenced, the results would inherently provide at least a relative abundance of the sequences present on the bead population following the emulsion PCR. For example, if the emulsion comprised 1,000,000 beads, then sequencing the products on 10,000 of those beads would provide a relative abundance. Even if each of the 10,000 sequences were different, then one would know that the relative abundance of each sequence was at most 1 in 10,000.

With regard to claim 45, Leamon teaches that empty beads can be separated from beads bound to copies of amplified product using a fluorescence cell sorter (column 27, lines 31-51) before delivering the beads to the array of chambers. Hence the determining at least the relative amounts of beads comprising one or more sequence features is performed "using" fluorescence activated cell sorting.

With regard to claim 46, Leamon teaches additional copies of primers not bound to the bead. See figure 6, and column 20, line 28 through column 21, line 20.

With regard to claims 47 and 48, Leamon teaches the nucleic acid molecules to be amplified can be either genomic DNA or cDNA. See column 21, lines 30-35.

With regard to claims 49 and 50, as explained in the discussion of "Bead Emulsion PCR Amplification" (column 20, line 28 through column 21, line 20), and as shown in figure 6, Leamon's method, even beginning with pure genomic DNA or cDNA, will inherently produce PCR products made from genomic DNA or cDNA, respectively,

during the initial cycle of PCR. Hence, beginning with the second cycle of PCR, the method utilizes PCR products made from genomic DNA or cDNA.

With regard to claim 51, Leamon teaches the method may be used in a number of applications, including "comparing genes or variations in genes on each of the two alleles present in a human subject" (column 9, lines 19-21). One of ordinary skill in the art would have inferred that for this application, the DNA would be derived from a single individual.

With regard to claim 52, Leamon teaches the method may be used in a number of applications, including "genotyping (comparing one or more genes in a first individual of a species with the same genes in other individuals of the same species)" (column 9, lines 25-27). One of ordinary skill in the art would have inferred that for this application, the DNA would be derived from a population of individuals.

With regard to claim 54, Leamon teaches an embodiment wherein, during the sequencing reaction, the nucleotides used are modified to contain a hapten, such as biotin (see column 40, beginning at line 58). Next, "[t]he addition of the modified nucleotide to the nascent primer annealed to the anchored substrate is analyzed" (column 40, lines 60-61). While biotin itself can be considered a "label", it is noted that Leamon teaches alternative haptens including cy3, cy5 and fluorescein (column 41, lines 14-16).

With regard to claim 59, the only distinction over claim 35 is in the final step, where instead of determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads, the method requires *isolating product*

beads which are bound to a plurality of copies of a first species of analyte DNA molecule from product beads which are bound to a plurality of copies of a second species of analyte DNA molecule.

Leamon teaches delivering the product beads to an array of reaction chambers, such that each chamber receives a single product bead. Hence, a bead bound to copies of one nucleic acid species is separated from a bead bound to copies of a second nucleic acid species. See claim 1.

With regard to claim 60, Leamon teaches that empty beads can be separated from beads bound to copies of amplified product using a fluorescence cell sorter (column 27, lines 31-51) before delivering the beads to the array of chambers. Hence the step of isolating is performed "using" fluorescence activated cell sorting.

With regard to claims 61 and 63, see column 24, lines 46-54: "Alternatively, the beads may be isolated and the DNA may be removed from each bead and sequenced."

With regard to claim 64, Leamon teaches a method comprising:

(a) forming aqueous compartments in a water-in-oil emulsion, wherein a plurality of compartments include a nucleic acid molecule, a bead capable of being linked to the nucleic acid molecule, and an aqueous solution comprising components necessary to perform nucleic acid amplification;

See claim 1: "delivering the fragmented nucleic acids into aqueous microreactors in a water-in-oil emulsion such that a plurality of aqueous microreactors comprise a single copy of a fragmented nucleic acid, a single bead capable of binding to the

fragmented nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification"

(b) amplifying the nucleic acid molecules in the compartments to form amplified product copies of the nucleic acid molecule;

See claim 1: "amplifying the fragmented nucleic acids in the microreactors to form amplified copies of said nucleic acids…".

and (c) capturing the amplified product copies to the bead in the compartments, thereby amplifying of the nucleic acid molecule.

See claim 1: "…and binding the amplified copies to beads in the microreactors".

With regard to claim 65, Leamon teaches that the preferred method of amplification is PCR. See column 23, lines 50-51, and see claim 5.

With regard to claim 66, Leamon teaches the addition of Tween 80, a detergent, to the PCR solution used to make the emulsion. See Example 5, columns 78-80. Hence, the emulsion comprised a detergent. Leamon also teaches in Example 15, column 86, the inclusion of Span 80, which is a detergent, in the emulsion oil (lines 20-25).

With regard to claim 67, Leamon teaches in Example 5, columns 78-80, "how to create a heat-stable water-in-oil emulsion containing about 3,000 PCR microreactors per microliter" (column 79, lines 15-17).

With regard to claim 68, Leamon teaches the nucleic acid molecules to be amplified can be either genomic DNA or cDNA. See column 21, lines 30-35.

With regard to claims 69 and 75, Leamon teaches at column 24, lines 63-66: "A high percentage of the beads may be "negative" (i.e., have no amplified nucleic acid template attached thereto) if the goal of the initial DNA attachment is to minimize beads with two different copies of DNA." In column 25, Leamon tests various fragment to bead ratios, including a fragment to bead ratio of 0.1, which according to the table would result in 90% of the beads having no fragments (R(0)). In an emulsion where 90% of the beads have no fragments, the compartments of the emulsion comprising beads represent a plurality of compartments containing on average less than one nucleic acid molecule. See also column 25, lines 57-60.

With regard to claim 70, the only distinction over claim 64 is the lack of a requirement for the beads. Hence, what Leamon teaches regarding claim 64 applies to claim 70 as well.

With regard to claims 71 and 74, Leamon teaches that the preferred method of amplification is PCR. See column 23, lines 50-51, and see claim 5.

With regard to claims 72 and 74, Leamon teaches in Example 5, columns 78-80, "how to create a heat-stable water-in-oil emulsion containing about 3,000 PCR microreactors per microliter" (column 79, lines 15-17).

With regard to claim 73, Leamon teaches that the amplified copies of the nucleic acid molecules become linked to a bead. See claim 1, and see figure 6 and the discussion of "Bead Emulsion PCR Amplification" (column 20, line 28 through column 21, line 20).

With regard to claim 76, the only distinction over claim 64 is the added requirement that *at least one of the compartments comprises a single nucleic acid template [and] a single bead* (i.e. not more than one of each).

Leamon clearly teaches this in claim 1: "such that a plurality of aqueous microreactors comprise a single copy of a fragmented nucleic acid, a single bead capable of binding to the fragmented nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification".

With regard to claim 77, Leamon teaches in Example 5, columns 78-80, "how to create a heat-stable water-in-oil emulsion containing about 3,000 PCR microreactors per microliter" (column 79, lines 15-17).

With regard to claim 78, in discussing the attachment of the nucleic acid templates to the DNA capture beads, Leamon teaches that the "DNA may be attached to the solid support, for example, via a biotin-streptavidin linkage". See column 17, lines 3-16.

With regard to claim 79, Leamon teaches a method comprising:

(a) fragmenting large template nucleic acid molecules to generate a plurality of fragmented nucleic acids;

See claim 1: "fragmenting large template nucleic acid molecules to generate a plurality of fragmented nucleic acids".

(b) delivering the fragmented nucleic acids into aqueous compartments in a water-in-oil emulsion such that a plurality of aqueous compartments comprise a single copy of a fragmented nucleic acid, a single bead capable of binding to the fragmented

nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification;

See claim 1: "delivering the fragmented nucleic acids into aqueous microreactors in a water-in-oil emulsion such that a plurality of aqueous microreactors comprise a single copy of a fragmented nucleic acid, a single bead capable of binding to the fragmented nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification".

(c) amplifying the fragmented nucleic acids in the compartments to form amplified copies of said nucleic acids and binding the amplified copies to beads in the compartments;

See claim 1: "amplifying the fragmented nucleic acids in the microreactors to form amplified copies of said nucleic acids and binding the amplified copies to beads in the microreactors".

(d) delivering the beads to an array,

See claim 1: "delivering the beads to an array".

and (e) performing a sequencing reaction simultaneously on a plurality of the reaction chambers.

See claim 1: "performing a sequencing reaction simultaneously on a plurality of the reaction chambers".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39, 43 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (U.S. Patent 7,323,305). On 5/30/2006, the application which issued as the '305 patent (application serial no. 10/767,779) was granted a petition to receive a change in the filing date from 22 September 2004 to 28 January 2004. The '305 patent claims priority to, among other provisional applications, provisional application 60/476,504 (filed June 6, 2003) and 60/465,071 (filed April 23, 2003).

The teachings of Leamon have been discussed in the rejection under 35 U.S.C. 102(e) above.

With regard to claim 43, Leamon does not teach the method of claim 35 wherein the step of determining is performed by hybridization to oligonucleotide probes which are differentially labeled. However, Leamon *does* teach an example where the identity of the amplified nucleic acids bound to the beads was determined by hybridization to

oligonucleotide probes which were differentially labeled, the only difference being that the amplification step was not performed in an emulsion, but rather in individual wells of a "picotiter plate". See Example 27, beginning in column 93. See especially column 96, lines 30-64 and column 98, line 29 through column 99, line 49.

It is noted that Leamon teaches that once single molecules of DNA template have been associated with single capture beads, the amplification of the molecules to produce clonal populations of molecules attached to the beads may be performed either by distributing the beads to individual wells of the picotiter plate (where the amplification occurs in the picotiter well, as was the case in Example 27) or by creating an emulsion with the beads along with the components needed for PCR, such that the amplification/attachment occurs in individual droplets of the emulsion (column 20, line 28 through column 21, line 29). In the latter case, after the beads are recovered from the emulsion, the beads may be distributed to the wells of a picotiter plate for sequencing (column 35, lines 4-5; column 76, lines 35-47: PTP = picotiter plate).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use differentially labeled probes to detect the sequences attached to the beads as prepared by the bead emulsion PCR strategy, Leamon taught doing the same for beads prepared by the "picotiter PCR" strategy. One of ordinary skill in the art would have realized that, regardless of which of the two strategies were used to produce the beads having the attached amplicons (both of which were taught in Leamon's disclosure), once the beads were in the wells of the picotiter plate, there was no difference between the beads produced by the two

amplification techniques. Hence, since Leamon taught the use of differentially labeled probes for detection of sequences attached to beads by the picotiter PCR technique, it would have been obvious to do the same thing with sequences attached to beads by the emulsion PCR technique.

With regard to claims 39 and 62, as discussed already, Leamon teaches at column 24, lines 46-54: "Alternatively, the beads may be isolated and the DNA may be removed from each bead and sequenced." Leamon does not teach that the DNA removed from (i.e. recovered) from the beads are further amplified.

It was well-known in the prior art of nucleic acid sequencing and manipulation to amplify nucleic acid. This can be seen from the background information provided by Leamon at column 2, lines 7-12, where it is stated that PCR "plays an integral part in obtaining DNA sequence information, amplifying minute amounts of specific DNA to obtain concentrations sufficient for sequencing."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, when practicing the embodiment taught by Leamon of removing the amplicons from the bead for sequencing, to further amplify the nucleic acid, so as to obtain more material.

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (U.S. Patent 7,323,305) in view of Becker (U.S. Patent 5,546,792). On 5/30/2006, the application which issued as the '305 patent (application serial no. 10/767,779) was granted a petition to receive a change in the filing date from 22 September 2004 to 28

January 2004. The '305 patent claims priority to, among other provisional applications, provisional application 60/476,504 (filed June 6, 2003) and 60/465,071 (filed April 23, 2003).

The teachings of Leamon have already been discussed.

With regard to claim 42, Leamon does not teach breaking emulsions by adding a detergent. However, Leamon *does* teach "[t]here are many methods of breaking an emulsion…and one of skill in the art would be able to select the proper method" (column 24, lines 4-7).

Becker teaches (Example II, columns 6-7) an example of using detergent to break down an oil and water emulsion.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use detergents to break the emulsion when practicing Leamon's methods as it was already known in the art that detergents could be used to break emulsions.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (U.S. Patent 7,323,305) in view of Macevicz (U.S. Patent 6,306,597). On 5/30/2006, the application which issued as the '305 patent (application serial no. 10/767,779) was granted a petition to receive a change in the filing date from 22 September 2004 to 28 January 2004. The '305 patent claims priority to, among other provisional applications, provisional application 60/476,504 (filed June 6, 2003) and 60/465,071 (filed April 23, 2003).

The teachings of Leamon have already been discussed.

With regard to claim 53, Leamon does not teach that the beads used in the emulsion amplification are magnetic beads.

Macevicz teaches attaching amplified target polynucleotides to magnetic beads "for ease of separating the target polynucleotide from other reagents used in the method" (column 8, lines 30-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use magnetic beads in the method disclosed by Leamon, since it was known in the prior art to use magnetic beads as solid supports for polynucleotides to facilitate their separation from other reagents used in nucleic acid methods.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637